



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-N-0230]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Examination of Online Direct-to-Consumer Prescription Drug Promotion

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-7285, or emailed to oir_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-New and title, Examination of Online Direct-to-Consumer Prescription Drug Promotion. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Examination of Online Direct-to-Consumer Prescription Drug Promotion--(OMB Control
Number 0910--New)

I. Background

Pharmaceutical products are launched and marketed in a number of new modalities and venues that did not exist a short time ago. Increasingly, prescription products are promoted to consumers online in such formats as banners, Web sites, and videos. The interactive nature of the Internet allows for features not possible with traditional media (i.e., print, radio, and television), such as scrolling information, popup windows, linking to additional information, and embedded videos. FDA regulations require that prescription drug advertisements include a "fair balance" of information about the benefits and risks of advertised products, both in terms of the content and presentation of the information (21 CFR 202.1(e)(5)(ii)). All prescription drug promotion that makes claims about a product must, therefore, also include risk information in a

"balanced" manner. Currently, there are a number of questions surrounding how to achieve "fair balance" in online direct-to-consumer (DTC) promotion.

A few studies have examined how well online DTC Web sites communicate benefit and risk information. Although content analyses demonstrate that most Web sites include information on side effects and contraindications (Ref. 1), risk information is often presented less prominently and in fewer locations on the Web site (Refs. 2, 3, and 4). Content analyses also suggest that risk information on DTC prescription drug Web sites is often incomplete (Ref. 5) and written at very high literacy levels (Ref. 6).

One study examined how users interact with prescription drug Web sites (Ref. 7). This study found that the placement of risk and benefit information on a Web site is an important factor in whether it achieves "fair balance." Specifically, participants' ability to find and accurately recall risk information was enhanced when risk and benefit information were presented separately and when risk information was presented on a higher order page (i.e., on a second-level page clearly linked from the homepage, or on the homepage).

This project is designed to test different ways of presenting prescription drug risk and benefit information on branded drug Web sites. This research is relevant to current policy questions and debate and will complement qualitative research we plan to conduct on issues surrounding social media. The series of studies described in this document will provide data that, along with other input and considerations, will inform the development of future guidance.

II. Comments

In the Federal Register of April 28, 2011 (76 FR 23821), FDA published a 60-day notice requesting public comment on the proposed collection of information. Seven statements were received, some of which included several comments.

(Comment 1) One comment expressed the opinion that DTC advertising will never present risk and benefit information in a balanced manner and therefore the government should take a stronger stand against DTC advertising.

(Response) This is outside the scope of this project, but we note that the overall purpose of the research is to improve consumer understanding of prescription drug advertising.

(Comment 2) The comment describes Web archiving technology and how it can be used to capture information from Web sites. They recommended we use their company's Web archiving services for regulatory activities and to conduct the study.

(Response) The sections of this comment that relate to how the company's services can be used for regulatory activities are beyond the scope of this project. The sections that relate to the research suggest that we could use Web archiving technology to create Web sites for the study; however, we plan to create new, unique, fictitious Web sites for the study to ensure familiarity with a particular Web site or brand does not have any influence on our findings.

(Comment 3) Two statements suggested additional information should be collected from participants. One statement suggested we use some of this additional information (prescription drug use) as a covariate.

(Response) Some of the additional information suggested is already included in the questionnaire (e.g., age, ethnicity, education level, and prescription drug use for the medical condition of interest). Although native language and whether participants are hearing or vision impaired are not directly assessed, participants must be capable of completing an intake questionnaire and core adult profile survey, both of which are written at an eighth grade reading level. Other additional information suggested will be included. Specifically, we will include level of Internet use and length of time from diagnosis with the medical condition of interest. In

addition, we will use prescription drug use for the medical condition of interest as a covariate in our analyses.

(Comment 4) One comment addressed the recruitment process, requesting that we disclose how participants will be recruited and recommending online recruitment.

(Response) We plan to recruit and conduct the study online.

(Comment 5) One comment recommended that caregivers also be included as participants.

(Response) To ensure that our participants are motivated to consider the information presented in the study and to conserve resources, we will limit our sample to people who have the medical condition of interest.

(Comment 6) One comment requested that we not apply the results of these studies to social media and mobile technology, as Web sites differ in a number of ways from other online contexts.

(Response) These studies are designed to address questions surrounding branded prescription drug Web sites and therefore the results will not be applied to social media and mobile technology.

(Comment 7) One comment requested that FDA publish the study design for the qualitative study mentioned in the Federal Register notice.

(Response) FDA plans to conduct 10 focus groups to investigate how consumers, patients, and caregivers use online health communities and social media sites to make health decisions, especially regarding prescription drugs. These focus groups received OMB approval on April 28, 2011 ("Examination of Online Direct-to-Consumer Prescription Drug Promotion,"

OMB control number 0910-0677). FDA will share the results of these focus groups when they become available.

(Comment 8) One comment suggested that the proposed samples sizes may not result in adequate statistical power.

(Response) We have conducted power analyses and will have sufficient sample to detect small to medium size effects with an alpha level of 0.05 and power of 0.90.

(Comment 9) One statement suggested that the proposed 2 x 2 + 1 design in Study 2 may limit an objective assessment of the effect of the variables in the control group. Another questioned the presence of the control group in Study 2, suggesting that it may confound the interpretation of results regarding the "prominence" manipulation. This statement suggested evaluating prominence in a separate part of the study.

(Response) Study 2 is designed to test two research questions: (1) To what extent does the presence of special features (e.g., personal testimonials, animated visuals) on a branded drug Web site influence consumer perceptions of a prescription drug and (2) to what extent does the prominence of risk information in special features on a branded drug Web site influence consumer perceptions of a prescription drug? Both research questions can be addressed within the same design without having to evaluate prominence in a separate design. The first research question will be tested by comparing responses of participants exposed to a Web site with a special feature to those who were not (the control group). The second research question will be tested by comparing responses of participants exposed to more prominently displayed risk information to those exposed to less prominently displayed risk information (i.e., the control condition would not be included in these analyses).

(Comment 10) One comment stated that the study outcome measures were not clear and recommended using validated measures.

(Response) The key outcome measures are risk comprehension, benefit comprehension, risk perceptions, and benefit perceptions. Where validated measures exist we will use them. Because the comprehension measures by necessity will be based on the information particular to each fictitious drug, these will be new measures; however, they will take the form of similar comprehension measures used by FDA and others in past research.

(Comment 11) One comment noted that we planned to conduct the studies with participants diagnosed with medical conditions like high cholesterol, seasonal allergies, depression, acid reflux, and high blood pressure, but suggested we also include participants with other medical conditions such as HIV and cancer and replicate the studies across different therapeutic areas.

(Response) As noted in the comment, we plan to conduct the studies with patients diagnosed with a range of medical conditions that differ in diagnosis, symptomatology, patient population, and treatment options. Because it is difficult to recruit participants from low-incidence samples such as those recommended, we do not plan to include these other medical conditions in the study. However, we will consider this for future studies and encourage replication across medical conditions by other researchers.

(Comment 12) One comment recommended that FDA not delay issuing draft Internet guidance until the results of the studies are known.

(Response) FDA does not intend to delay issuing draft guidance because of this research.

(Comment 13) One comment suggested that FDA policy should not categorically prohibit the use of hyperlinks to provide risk information.

(Response) Because this comment addresses issues of policy and not the current research, this comment is outside the scope of this project.

(Comment 14) One comment suggested that, rather than focus on a single branded drug Web site, the studies should take into account the multiple executional elements of Internet drug promotion and how online promotional executions are affected by the broader health information environment. The comment argues that this is necessary because risk and benefit comprehension is affected not only by the specifics of one branded drug Web site but also by other health information found online and elsewhere.

(Response) The regulations these studies address do not apply to the broader online health information environment; rather, each individual branded drug Web site needs to achieve fair balance. The fictitious branded drug Web sites used in the studies will include multiple executional elements; however, only one variable will be manipulated at a time in order to maintain experimental control.

(Comment 15) One comment recommended we take advantage of other researchers who can help revise the study design.

(Response) We obtained comments from peer reviewers and incorporated their suggestions in the new design.

(Comment 16) One comment noted that there are numerous issues that this research does not address, including online data mining by pharmaceutical companies, techniques of personalization for targeted digital pharmaceutical and health marketing, and pharmaceutical marketing's "exploitative" approach to social media. The comment criticized the focus on branded drug Web sites, as the online marketing environment encompasses newer technology.

(Response) Although there are several other issues surrounding prescription drug advertising online, such as privacy concerns, this is not the purview of the current research. This research is not designed to "assess the full impact of digital drug marketing" or document pharmaceutical marketing practices but rather to address specific issues regarding implementation of "fair balance" regulations for branded prescription drug Web sites. We note that no one study can address all relevant questions and encourage others to pursue research in this area to supplement the proposed research.

Although the online landscape is much broader than Web sites, Web sites continue to be a major source of information for consumers (e.g., a recent survey found that 49 percent of respondents who went online for prescription drug information reported seeking this information on a specific brand's Web site (Ref. 8)) and, as noted previously in this document, there is not much relevant research on branded prescription drug Web sites.

(Comment 17) One comment suggested that the study use eye tracking and neuromarketing methods.

(Response) Because the comment does not specify why eye tracking and neuromarketing should be used in this research beyond noting that the pharmaceutical industry employs these methods, it is difficult to understand how the current research would benefit from these methods. Neuromarketing, for instance, may tell us that participants prefer one Web site over another. While this is relevant information from a marketing perspective, from a regulatory perspective it is comprehension, and not preference, that is the important outcome to assess.

(Comment 18) One comment requested additional information on the study. Issues not already addressed previously in this document include hypotheses, how the risk information will be portrayed, whether the Web site will be viewed under controlled conditions, how the

participants' perceptions and understanding of the risks and benefits will be assessed, and the statistical analyses to be performed.

(Response) As noted in the 60-day Federal Register notice, the questionnaire is available upon request; this demonstrates how participants' perceptions and understanding will be assessed. We intend to manipulate how the risk information will be portrayed; please see the study design. Participant will complete the study online, not under controlled conditions. We will ask about the type of device they are using to view the Web site and can control for this if necessary. Hypotheses and statistical analyses are included in this document.

(Comment 19) One comment recommends testing the use of hyperlinks to risk information in the first study. The comment states that this would be useful in developing guidance for social media as well.

(Response) We have revised the design in Study 1 so that the risk visibility manipulation now tests the use of hyperlinks to risk information. We note that this study focuses on prescription drug Web sites aimed at consumers. As discussed in a previous comment, the results of these studies will be applied in this context only and not to social media.

(Comment 20) One comment asks for more detail regarding the checklist and animated spokesperson to be used in the first study.

(Response) The Study 1 risk formats were chosen based on the risk communication literature. Risk communication studies have found that making risk information less dense (e.g., bulleted lists), more visual (e.g., checklists), and audible (e.g., spokesperson) might increase comprehension. Thus, we want to test formats that are consistent with risk communication best practices. The checklist will be more visual and pronounced than a typical bulleted list. The animated spokesperson will include an audio component.

(Comment 21) One comment recommended that FDA follow FDA's 2009 Draft Guidance on Presenting Risk Information when deciding which risk information should be included in the special features in Study 2.

(Response) FDA will consider this guidance when designing the study stimuli.

(Comment 22) One comment questioned the usefulness of the Study 3 design.

(Response) We have redesigned the third study to ensure it addresses relevant questions in online prescription drug promotion. Please see the revised study design in this document.

III. Revised Study Design

This research will be conducted in three concurrent studies. The design and hypotheses for each study are outlined as follows. We will use ANOVAs, planned comparisons, and regressions to test hypotheses.

The purpose of Study 1 is to investigate whether the presentation of risk information on branded drug Web sites influences consumers' perceptions and understanding of the risks and benefits of the product. In Study 1, we will examine the format (e.g., whether the risk information is presented in a paragraph or as a bulleted list) and visibility of risk information on a prescription drug Web site. Risk visibility will be manipulated by having the risk information on the homepage; having the risk information on the homepage with a signal to scroll; or having a hyperlink, with a signal to click on the link, on the homepage that leads to a secondary page with the risk information. The signal will direct participants to the important safety information. Participants will be randomly assigned to experimental conditions in a factorial design as follows:

Table 1.--Study 1 Proposed Design (3 x 5)

Risk Visibility	Format				
	Paragraph	Bullet List	Checklist	Highlighted Box	Animated Spokesperson
On Homepage					
On Homepage with Signal					
On Secondary Page with Signal					

A. Study 1 Hypotheses

1. Locating risk information on the homepage (with or without a signal) will lead consumers to have greater perceived risk and greater risk comprehension than locating this information on a secondary page with a hyperlink. Locating risk information on the homepage with a signal will lead consumers to have greater perceived risk and greater risk comprehension than locating this information on the homepage without a signal.

2. Presenting risk information in a bulleted list or checklist format will lead consumers to have greater perceived risk and greater risk comprehension than presenting this information in paragraph format.

3. Presenting risk information in a highlighted box format will lead consumers to have greater perceived risk and greater risk comprehension than presenting this information in bulleted list, checklist, or paragraph format.

4. We have competing hypotheses for the animated spokesperson. If the use of audio increases attention to the animated spokesperson, then presenting risk information via an animated spokesperson will lead consumers to have greater perceived risk and greater risk comprehension than presenting this information in any other format. If the animated spokesperson distracts consumers and/or the preset pace of the audio presentation is difficult for consumers to follow, then presenting risk information via an animated spokesperson will

lead consumers to have lower perceived risk and lower risk comprehension than presenting this information in any other format.

The purpose of Study 2 is to investigate how special visual features on branded drug Web sites influence perceptions and understanding of the risks and benefits of the product. The special features we will examine are a personal testimonial video and an animated mechanism of action visual. Benefit information will be presented in either a personal testimonial video, an animated mechanism of action visual, or in text (the control). We will examine these special features in the context of the prominence of the presentation of risk information in two levels; more prominent and less prominent. An example of a more prominent display of risk information might involve including the risks as part of the spoken testimonial, whereas a less prominent display may involve a scrolling text of the risks after the animated video. We will include a control condition in which participants view a Web page with no special features. Participants will be randomly assigned to experimental conditions in a factorial design as follows:

Table 2.--Study 2 Proposed Design (2 x 2 + 1)

Special Features			
Risk Presentation	Personal Testimonial	Animated Visual	Control Group
Prominent			
Less Prominent			

B. Study 2 Hypotheses

1. The presence of any special feature will lead consumers to have lower perceived risk, greater perceived efficacy, greater benefit comprehension, and greater intentions to ask their doctor about the drug than the absence of these features.

2. More prominently displayed risk information will lead consumers to have greater perceived risk and greater risk comprehension than less prominently displayed risk information.

The revised Study 3 design tests whether participants are misled by a link from a branded prescription drug Web site to a disease awareness Web site with off-label information, and whether the presence of context attenuates this potential effect. Participants will be randomly assigned to experimental conditions in a factorial design as follows:

Table 3.--Study 3 Revised Design (4 x 1)

Context			
No Link (Control)	None	External Only	External & Not Sponsored

The three context conditions will include a link. For example, "For more information about Disease X, please visit [link]." An example of the "none" context condition is, "if the link is clicked, there is an interim page that says 'Loading.' " An example of the "external only" context is, "if the link is clicked, there is an interim page that says 'You are leaving the Drug X Web site and entering an external Web site.' " An example of the "external and not sponsored" context is "if the link is clicked, there is an interim page that says 'You are leaving the Drug X Web site and entering an external Web site not controlled or endorsed by Pharmaceutical Company Y.' "

C. Study 3 Hypotheses

1. Participants who view the link to external information, compared to those who do not, will have greater perceived efficacy and lower correct benefit comprehension.

2. This effect may be attenuated by context, such that participants who view the link without context, compared to those who view the link with either type of context, will have

greater perceived efficacy and lower correct benefit comprehension. We will explore whether the type of context (external only vs. external and not sponsored) affects perceived efficacy and benefit comprehension.

In these three studies, participants will be randomly assigned to view one version of a (fictitious) prescription drug Web site. After viewing the Web site, participants will answer a series of questions about the drug. We will test how the manipulations affect outcomes such as perceived efficacy, perceived risk, behavioral intention, and accurate understanding of the benefit and risk information. In each study, the fictitious prescription drug will be for the treatment of a high prevalence medical condition and modeled on an actual drug used to treat that condition. Participants will be consumers who have been diagnosed with the medical condition of interest. For instance, the medical conditions may be high cholesterol and seasonal allergies for Study 1, high blood pressure and acid reflux disease for Study 2, and depression for Study 3. Interviews are expected to last no more than 25 minutes (the questionnaire is available upon request). This will be a one-time (rather than annual) collection of information.

FDA estimates the burden of this collection of information as follows:

Table 4.--Estimated Annual Reporting Burden¹

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Screeners	16,000	1	16,000	0.03 (2 minutes)	533
Pretests	1,200	1	1,200	0.33 (20 minutes)	400
Study 1	6,000	1	6,000	0.42 (25 minutes)	2,500
Study 2	2,000	1	2,000	0.42 (25 minutes)	833
Study 3	1,000	1	1,000	0.42 (25 minutes)	417
Total					4,683

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

IV. References

The following references have been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Macias, W. and L. Stavchansky Lewis, "How Well Do Direct-to-Consumer (DTC) Prescription Drug Web Sites Meet FDA Guidelines and Public Policy Concerns?" Health Marketing Quarterly, vol. 22, pp. 45-71, 2005.
2. Hicks, K.E., M.S. Wogalter, and W.J. Vigilante, Jr., "Placement of Benefits and Risks in Prescription Drug Manufacturers' Web Sites and Information Source Expectations," Drug Information Journal, vol. 39, pp. 267-278, 2005.
3. Huh, J. and B.J. Cude, "Is the Information 'Fair and Balanced' in Direct-to-Consumer Prescription Drug Web Sites?" Journal of Health Communication, vol. 9, pp. 529-540, 2004.

4. Sheehan, K.B., "Direct-to-Consumer (DTC) Branded Drug Web Sites Risk Presentation and Implications for Public Policy," Journal of Advertising, vol. 36, pp. 123-135, 2007.

5. Davis, J.J., E. Cross, and J. Crowley, "Pharmaceutical Web Sites and the Communication of Risk Information," Journal of Health Communication, vol. 12, pp. 29-39, 2007.

6. Naik, S. and S.P. Desselle, "An Evaluation of Cues, Inducements, and Readability of Information on Drug-Specific Web Sites," Journal of Pharmaceutical Marketing and Management, vol. 17, pp. 61-81, 2007.

7. Vigilante, Jr., W.J., and M.S. Wogalter, "Assessing Risk and Benefit Communication in Direct-to-Consumer Medication Web Site Advertising," Drug Information Journal, vol. 39, pp. 3-12, 2005.

8. Prevention Magazine. 14th Annual Survey of Consumer Reactions to DTC Advertising of Prescription Medicines, Emmaus, PA: Rodale, Inc., 2011.

Dated: December 13, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.